

this Request is a copy of the two Information Disclosure Statements, along with the accompanying Forms PTO-1449 and cited references. Also attached are copies of stamped postcards, indicating that the attached papers and references were received by the Office on October 26, 2001, and January 22, 2002. Because the attached papers and references were timely filed in complete form, Applicants believe that no petition or fee is due for re-submission of them. However, if any petition or fee is required, please grant the petition and charge the fee to our Deposit Account No. 06-0916.

## II. *Drawings*

The Office states that the drawings filed April 17, 2001, are not in the PTO file, and requests that Applicants re-submit them. (Office Action at paragraph 3.) Attached to this Request is a copy of the 12 sheets of drawings (12 figures) submitted with the application on April 17, 2001. Also attached is a copy of a stamped postcard, indicating that the 12 sheets of drawings were filed by Applicants, and received by the Office, with the application on April 17, 2001. Because the attached papers were timely filed in complete form, Applicants believe that no petition or fee is due for re-submission of them. However, if any petition or fee is required, please grant the petition and charge the fee to our Deposit Account No. 06-0916.

## III. *Restriction Requirement*

The Office makes the Restriction Requirement FINAL. (Office Action at paragraph 4.) Applicants respectfully submit that the claims of elected Group I are related to those of non-elected Group II as a product and a process of using. Furthermore, the claims of elected Group I

are related to those of non-elected Group II as a product and a process of making. Applicants respectfully submit that, in accordance with MPEP § 821.04, the non-elected process claims of Groups II and III should be rejoined with the product claims of Group I once one or more product claims are found to be allowable.

IV. *Rejections Under 35 U.S.C. § 102*

A. Uhlmann et al.

The Office rejects claims 1-9, 20, 21, and 31-85 under 35 U.S.C. § 102(b) as anticipated by Uhlmann et al. (*Nucleosides and Nucleotides*, 1997). (Office Action at paragraph 5.) The Office asserts that Uhlmann teaches polyamide nucleic acids with N-(2-aminoethyl)glycine units, and that this teaching anticipates present claims 1-9, 20, 21, and 31-85. The Office does not identify the specific compound in Uhlmann that supposedly anticipates the compounds of claims 1-9, 20, 21, and 31-85. Applicants respectfully submit that Uhlmann does not disclose a compound according to present claims 1-9, 20, 21, and 31-85, and thus does not anticipate these claims.

Present claim 1, and thus its dependent claims 2-9, 20, 21, and 31-85, recite a PNA derivative that carries one or more phosphoryl radicals at the N-terminus of the PNA backbone. The structures disclosed by Uhlmann on pages 603 (the unmodified PNA), at the bottom of page 604, and on page 606, do not anticipate any of claims 1-9, 20, 21, and 31-85 because, among other reasons, they do not possess a phosphoryl radical at the N-terminus.

With regard to the structure disclosed by Uhlmann at the top of page 604 (PHONA) and on page 607 (synthesis of PHONA), Applicants submit that the PHONA of Uhlmann cannot be constructed from the formula recited in present claim 1. For example, the phosphonate ester

linkage present in the PHONA structure of *Uhlmann* is not a possible linkage according to the formula recited in present claim 1. Further, the PHONA structure of *Uhlmann* contains a C-terminal  $\text{CH}_2\text{-P(O)(OR)O}^-$  radical. This type of radical cannot be constructed from present claim 1 because the formula of present claim 1 does not encompass a C-terminal phosphate group. Accordingly, the PHONA disclosed by *Uhlmann* on page 604 does not anticipate claims 1-9, 20, 21, and 31-85.

With regard to the structure disclosed by *Uhlmann* at the bottom of page 603 (DNA-PNA chimera), Applicants submit that the DNA-PNA chimera of *Uhlmann* cannot be constructed from the formula recited in present claim 1. For example, the DNA-PNA chimera of *Uhlmann* does not possess a group that satisfies element "Z" of formula I of present claim 1. Accordingly, the DNA-PNA chimera disclosed by *Uhlmann* on page 603 does not anticipate claims 1-9, 20, 21, and 31-85.

In view of the above comments, Applicants submit that *Uhlmann* does not disclose a PNA derivative according to present claim 1. Because claims 2-9, 20, 21, and 31-85 depend from claim 1, and thus include all of the elements of the PNA derivative recited in claim 1, *Uhlmann* likewise does not disclose a PNA derivative according to present claims 2-9, 20, 21, and 31-85. Therefore, Applicants respectfully request that the Office reconsider and withdraw the rejection of claims 1-9, 20, 21, and 31-85 as anticipated under 35 U.S.C. § 102(b) by *Uhlmann*.

B. Breipohl et al.

The Office rejects claims 1-12, 21, and 31-85 under 35 U.S.C. § 102(b) as anticipated by Breipohl et al. (U.S. Patent No. 6,046,306). (Office Action at paragraph 6.) The Office asserts

that *Breipohl* teaches labelled polyamide nucleic acids, and that this teaching anticipates present claims 1-12, 21, and 31-85. The Office does not identify the specific compound in *Breipohl* that supposedly anticipates the PNA derivative of claims 1-12, 21, and 31-85. Applicants respectfully submit that *Breipohl* does not disclose a PNA derivative according to present claims 1-12, 21, and 31-85.

Present independent claim 1 recites a PNA derivative which carries one or more phosphoryl radicals at the N-terminus of the PNA backbone. Claims 2-12, 21, and 31-80 all depend, either directly or ultimately, from claim 1. Thus, if *Breipohl* does not anticipate claim 1, it does not anticipate claims 2-12, 21, and 31-85.

Applicants submit that *Breipohl* does not disclose a PNA derivative which carries one or more phosphoryl radicals at the N-terminus of the PNA backbone. As mentioned above, the Office does not identify any such PNA derivative. In view of the lack of disclosure of such a PNA derivative, *Breipohl* does not anticipate claim 1. Accordingly, *Breipohl* does not anticipate claims 2-12, 21, and 31-85. Therefore, Applicants respectfully request that the Office reconsider and withdraw the rejection of claims 1-12, 21, and 31-85 as anticipated under 35 U.S.C. § 102(b) by *Breipohl*.

V. *Rejections Under 35 U.S.C. § 103*

A. *Uhlmann et al.* in view of *Weiler et al.*

The Office rejects claims 22 and 23 under 35 U.S.C. § 103(a) as unpatentable over *Uhlmann et al.* in view of *Weiler et al.* (Nucl. Acids Res. 1997). (Office Action at paragraph 7.)

The Office relies on *Uhlmann* for the teaching of polyamide nucleic acids with N-(2-

aminoethyl)glycine units, but asserts that *Uhlmann* does not disclose microarray supports for these PNAs. The Office asserts, however, that *Weiler* teaches the construction of PNA microarrays. The Office then concludes that it would have been obvious to construct microarrays using *Uhlmann's* PNAs. Applicants respectfully submit that, regardless of whether it would be obvious to use *Uhlmann's* PNAs in *Weiler's* microarrays, the combination of *Uhlmann* and *Weiler* does not render present claims 22 and 23 obvious.

Claims 22 and 23 depend from claim 1. Thus, if the PNA derivative of claim 1 is not disclosed or suggested by the combination of *Uhlmann* and *Weiler*, then claims 22 and 23 cannot be obvious either.

For the reasons discussed above, Applicants submit that *Uhlmann* does not disclose or suggest the PNA derivative of claim 1. Thus, to render claims 22 and 23 obvious, *Weiler* must at least disclose or suggest the PNA derivative of claim 1, in addition to teaching the use of such a PNA derivative in microarrays. Applicants submit that *Weiler* does not teach either of these.

*Weiler* describes the synthesis of macroscopic arrays of unmodified PNAs on membranes, and various hybridization studies based on these arrays. However, *Weiler* does not disclose or suggest the PNA derivative of present claim 1.

Furthermore, *Weiler* is limited to macroarrays, whereas present claim 22 is directed to microarrays. The differences between the macroscopic array described by *Weiler* and the microarrays of claim 23 is more than just semantic in nature, due both to the inherently different chemistry and technology requirements for their synthesis, as well as the possibility of massively parallel hybridization experiments using microarrays (which are not possible using macroarrays).

Finally, *Weiler* does not disclose or suggest the synthesis, or advantages, of arrays of PNA

derivatives carrying one or more phosphoryl radicals at their N-termini.

For at least these reasons, Applicants submit that the combination of *Uhlmann* and *Weiler* fails to render present claims 22 and 23 obvious. Accordingly, Applicants submit that present claims 22 and 23 are patentable under 35 U.S.C. § 103(a) over the combination of *Uhlmann* and *Weiler*.

B. Breipohl et al. in view of Weiler et al.

The Office rejects claims 22 and 23 under 35 U.S.C. § 103(a) as unpatentable over *Breipohl et al.* in view of *Weiler et al.* (Office Action at paragraph 8.) The Office relies on *Breipohl* to teach labelled polyamide nucleic acids. The Office asserts that *Breipohl* does not teach microarrays, but that *Weiler* teaches construction of PNA microarrays. The Office then concludes that it would have been obvious to construct microarrays using *Breipohl's* PNAs. Applicants respectfully submit that, regardless of whether or not it would be obvious to use *Breipohl's* PNAs in *Weiler's* microarrays, the combination of *Breipohl* and *Weiler* does not render present claims 22 and 23 obvious.

As discussed above, to render claims 22 and 23 obvious, the combination of *Breipohl* and *Weiler* must disclose or suggest the PNA derivative of present claim 1. For the reasons discussed above, Applicants submit that *Breipohl* does not disclose or suggest the PNA derivative of claim 1. Thus, to render claims 22 and 23 obvious, *Weiler* must at least disclose or suggest the PNA derivative of present claim 1, in addition to teaching the use of such a PNA derivative in microarrays. Applicants submit that *Weiler* does not teach either of these.

*Weiler* describes the synthesis of a macroscopic arrays of unmodified PNAs on membranes, and various hybridization studies based on these arrays. However, *Weiler* does not

disclose or suggest the PNA derivative of present claim 1.

Furthermore, as discussed above, *Weiler* is limited to macroarrays, whereas present claim 22 is directed to microarrays. The differences between the macroscopic array described by *Weiler* and the microarrays of claim 22 is more than just semantic in nature, due both to the inherently different chemistry and technology requirements for their synthesis, as well as the possibility of massively parallel hybridization experiments using microarrays (which are not possible using macroarrays).

Finally, *Weiler* does not disclose or suggest the synthesis, or advantages, of arrays of PNA derivatives carrying one or more phosphoryl radicals at their N-termini.

For at least these reasons, Applicants submit that the combination of *Breipohl* and *Weiler* fails to render present claims 22 and 23 obvious. Accordingly, Applicants submit that present claims 22 and 23 are patentable under 35 U.S.C. § 103(a) over the combination of *Breipohl* and *Weiler*.

C. Uhlmann *et al.* in view of Manoharan *et al.*

The Office rejects claims 13-15 under 35 U.S.C. § 103(a) as unpatentable over Uhlmann *et al.* in view of Manoharan *et al.* (U.S. Patent No. 6,043,352). (Office Action at paragraph 9.) The Office relies on *Uhlmann* for the teaching of polyamide nucleic acids with N-(2-aminoethyl)glycine units. The Office asserts that *Uhlmann* does not disclose a pharmaceutical composition comprising a PNA, or targeting of a PNA to the HA ras translation start site, but that *Manoharan* teaches use of PNAs, and in particular PNAs specific for the HA ras translation start site, in pharmaceutical compositions. The Office then concludes that it would have been obvious to make a pharmaceutical composition comprising a PNA according to *Uhlmann* that is specific

for the HA ras translation start site, as taught by *Manoharan*. Applicants respectfully submit that, regardless of whether or not it would be obvious to use *Uhlmann's* PNAs in *Manoharan's* pharmaceutical compositions, the combination of *Uhlmann* and *Manoharan* does not render present claims 13-15 obvious.

Claims 13-15 depend from claim 1. Thus, to render claims 13-15 obvious, *Uhlmann* or *Manoharan* must disclose or suggest the PNA derivative of claim 1. For the reasons discussed above, Applicants submit that *Uhlmann* does not disclose or suggest a PNA derivative according to claim 1. Thus, in order for the combination of *Uhlmann* and *Manoharan* to render claims 13-15 obvious, *Manoharan* must disclose or suggest at least a PNA derivative according to claim 1. Applicants submit that *Manoharan* does not disclose or suggest such a PNA derivative. The Office has not identified any such teaching, and Applicants have found no such teachings in *Manoharan*.

Because the combination of *Uhlmann* and *Manoharan* fails to disclose or suggest the PNA derivatives of present claim 1, the combination fails to render the PNA derivatives of present claim 1 obvious. Accordingly, the combination of *Uhlmann* and *Manoharan* cannot render the PNA derivatives of claims 13-15 obvious. For at least this reason, Applicants submit that claims 13-15 are patentable under 35 U.S.C. § 103(a) over the combination of *Uhlmann* and *Manoharan*. Therefore, Applicants respectfully request that the Office reconsider and withdraw the rejection of claims 13-15 under 35 U.S.C. § 103(a) as unpatentable over *Uhlmann* in view of *Manoharan*.



VI. *Conclusion*

Applicants submit that present claims 1-15, 20-23, and 31-85 are neither anticipated nor rendered obvious by the cited references. Therefore, Applicants request that the Office withdraw the rejections set forth in the Office Action, rejoin method claims 16-19 and 24-30, and permit this application to issue as a U.S. patent in due course. If the Office believes anything further is necessary in order to place this application in even better condition for allowance, Applicants request that their undersigned representative be contacted at the telephone number or e-mail address below to discuss the remaining issues.

Please grant any extension of time required to enter this response and charge any required fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, L.L.P.

By: 

Matthew T. Latimer

Reg. No. 44,204

571-203-2714

[matthew.latimer@finnegan.com](mailto:matthew.latimer@finnegan.com)

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Attachments:

Re-submission of IDS/PTO-1449/references  
of October 26, 2001 and January 22, 2002

Re-submission of Figures 1-12

FINNEGAN  
HENDERSON  
FARABOW  
GARRETT &  
DUNNER LLP

1300 I Street, NW  
Washington, DC 20005  
202.408.4000  
Fax 202.408.4400  
[www.finnegan.com](http://www.finnegan.com)